CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. Patent Application No. 09/457,048, filed December 7, 1999 now abandoned which application is a continuation of U.S. Patent Application No. 08/898,501, filed July 22, 1997, now issued as U.S. Pat. No. 6,027,890; which application is a continuation-in-part of U.S. Patent Application No. 08/787,521, filed January 22, 1997, now abandoned; which application claims the benefit of U.S. Provisional Patent Application No. 60/010,436, filed January 23, 1996, and U.S. Provisional Patent Application No. 60/015,402, filed March 21, 1996, which applications are incorporated herein by reference in their entirety.

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Please insert the enclosed "Sequence Listing" immediately after the section of the specification entitled "Abstract of the Disclosure" on page 151.

Please replace the paragraph beginning at page 112, line 10, with the following rewritten paragraph:

Preparation of 2,4,6-trichlorotriazine derived oligonucleotides: 1000 µg of 5'-terminal amine linked oligonucleotide (5'-hexylamine-TGTAAAACGACGGCCAGT-3") (SEQ ID NO: 1) are reacted with an excess recrystallized cyanuric chloride in 10% n-methyl-pyrrolidone alkaline (pH 8.3 to 8.5 preferably) buffer at 19 to 25- C for 30 to 120 minutes. The final reaction conditions consist of 0.15 M sodium borate at pH 8.3, 2 mg/ml recrystallized cyanuric chloride and 500 ug/ml respective oligonucleotide. The unreacted cyanuric chloride is removed by size exclusion chromatography on a G-50 Sephadex column.

A2

Please replace the paragraph beginning at page 124, line 27, with the following rewritten paragraph:

ODNs complementary (5'-CCTTAGGACAGTCTTCTTCACGC; SEQ ID NO: 2) to conserved or hypervariable regions of the 16S ribosomal RNA (rRNA) of Porphyromonas gingivalis (Pg), were synthesized on either an ABI 380B or a MilliGen 7500 automated DNA synthesizer using the standard cyanoethyl-N,N-diisopropylamino-phosphoramidite (CED-phosphoramidite) chemistry. Amine tails were incorporated onto the 5'-end using the commercially available N-monomethoxytritylaminoihex-6-yloxy-CED-phosphoramidite. ODNs

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with 5'-monomethoxytritryl groups were chromatographed by HPLC using a Hamilton PRP-1 (7.0 x 305 mm) reversed-phase column employing a gradient of 5% to 45% CH3CN in 0.1 M Et3NH+OAc-, pH 7.5, over 20 min. After detritylation with 80% acetic acid, the ODN s were precipitated by addition of 3 M sodium acetate and 1-butanol. Analytical checks for the quality of the ODNs were done by ion-exchange HPLC using a Toso-Haas DEAE-NPR column and by denaturing polyacrylamide gel electrophoresis (PAGE).

A3 cond

Please replace the paragraph beginning at page 127, line 1, with the following rewritten paragraph:

F. Solid Support cDNA Synthesis for Gene Expression Assay

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Oligo DMO 596 5'- ACTACTGATCAGGCGCGCCTTTTTTTTTTTTTTTTTT -3' (SEQ ID NO: 3) spacer Asc I (poly dT)20

Please replace the paragraph beginning at page 127, line 24, with the following rewritten paragraph:

One nylon bead bearing the covalently linked oligonucleotide, 5'-ACTACTGATCAGGCGCGCCTTTTTTTTTTTTTTTTTT - 3' (SEQ ID NO: 4) (GenSet, La Jolla, CA), is added to,10,ug total cellular RNA, diluted in enough RNase-free water to cover the bead, in a sterile 1.5 ml microfuge tube (Fisher Scientific). The RNA and bead are incubated at 65C for 5 minutes. An equal volume of 2X mRNA hybridization buffer consisting of 50,mM Tris pH 7.5 , 1M NaCl (Fisher Scientific) and 20,ug/ml acetylated-BSA (New England Biolabs, Beverly, MA) is added to each tube and the tubes rocked gently for 2 hours at room temperature. The supernatant is removed and the bead is then washed three times in 1X mRNA hybridization buffer. After the final wash is complete, a reverse transcription mix consisting of 1X MMLV-reverse transcriptase buffer, 1,mM dNTP mix, 2,mM DTT (Life Technologies), 20 units Rnasin (Promega. Madison, WI)and 10,ug/ml acetylated-BS (New England Biolabs) is added to each tube followed by addition of 600 units MMLV-reverse transcriptase(Life Technologies). This reaction is rocked gently at 42°C for 2 hours. 1 unit RNase H (Boehringer-Mannheim. Indianapolis, IN) is then added and the reaction allowed to continue for another 0.5 hour. The supernatant is again removed

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and each bead is washed three times in 10 mM Tris pH 8.0, 1 mM EDTA pH 8(Fisher Scientific). Remaining RNA template is removed by boiling the beads in TE with 0.01% SDS (Fisher Scientific).

Please replace the paragraph beginning at page 128, line 8, with the following rewritten paragraph:

The nylon solid support was then hybridized with 100 nanograms per ml of the following tagged oligonucleotide probes

(5'-GAACTCAAACCTCTGGAGGAAGTG-3', IL-2,	(SEQ ID NO: 5)
5'- CAGTGCAGAGGCTCGCGAGCTATA-3',IFN-gamma	(SEQ ID NO: 6)
5'-CTTGACCATGATGGCCAGCCACTA-3', GM-CSF	(SEQ ID NO: 7)
5'- CATTCCCACGGTCACTGCCATCTC-3', c-fos	(SEQ ID NO: 8)
5'- GCGACTGTGCTCCGGCAGTTCTAC-3', IL-4	(SEQ ID NO:9)
5'- GTGGTTCATCGACGATGCCACGAA-3', PKC-gamma	(SEQ ID NO: 10)
5'- GAGCTCATGTACCCACCTCCGTAC-3', CTLA4/CD28	(SEQ ID NO: 11)
5'- ATCTTCGTGCAGCCGCCCTCACTG-3', GMP kinase)	(SEQ ID NO: 12)

Please replace the paragraph beginning at page 129, line 19, with the following rewritten paragraph:

A "target" oligonucleotide (DMO501: 5'-TTGATTCCCAATTATGCGAAGGAG-3'; SEQ ID NO: 13) was immobilized on a set of solid supports. ODN-beads (3/32nd inch diameter) were prepared as previously described (Van Ness et al., *Nucl. Acids Res. 19*:3345, 1991). The ODN-beads contained 0.01 to 1.2 mg/bead of covalently immobilized ODN. DMO578 is the complement to DMO501 (perfect complement). DMO1969 is the complement to DMO501 with a G--->T change at position 11. DMO1971 is the complement to DMO501 with a A--->T change at position 12. Each probe oligonucleotide was labeled with either BIODIPY, TAMRA or Texas Red. Hybridization reactions were assembled in 3 M GuSCN, 0.01 M Tris pH 7.6, 5 mM EDTA at 50 ng/ml respective probe. Equal molar ratios of each probe type were used in each hybridization in the presence of 3 solid supports per tube. Hybridizations are performed at 42°C for 30 minutes with constant agitation. The beads were washed twice with 3 M GuSCN at 42°C and then with

A7 cond SDS/FW 5 times.

Please replace the section at page 5, line 14 to page 6, line 9, with the following revised section:

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A, 1B, and 1C depict the flowchart for the synthesis of pentafluorophenyl esters of chemically cleavable mass spectroscopy tags, to liberate tags with carboxyl amide termini.

Figures 2A, 2B, and 2C depict the flowchart for the synthesis of pentafluorophenyl esters of chemically cleavable mass spectroscopy tags, to liberate tags with carboxyl acid termini.

A8 Figures 3A, 3B, and 3C; 4A, 4B, and 4C; 5A, 5B, and 5C; 6A, 6B, and 6C; and 8A, 8B, and 8C depict the flowchart for the synthesis of tetrafluorophenyl esters of a set of 36 photochemically cleavable mass spectroscopy tags.

Figures 7A, 7B, and 7C depict the flowchart for the synthesis of a set of 36 amine-terminated photochemically cleavable mass spectroscopy tags.

Figure 9 depicts the synthesis of 36 photochemically cleavable mass spectroscopy tagged oligonucleotides made from the corresponding set of 36 tetrafluorophenyl esters of photochemically cleavable mass spectroscopy tag acids.

Figures 10A and 10B depict the synthesis of 36 photochemically cleavable mass spectroscopy tagged oligonucleotides made from the corresponding set of 36 amine-terminated photochemically cleavable mass spectroscopy tags.

Figure 11 illustrates the simultaneous detection of multiple tags by mass spectrometry.

Figure 12 shows the mass spectrogram of the alpha-cyano matrix alone.

Figure 13 depicts a modularly-constructed tagged nucleic acid fragment.

Figure 14 is a schematic representation of an array interrogation system using Matrix Assisted Laser Desorption Ionization (MALDI) mass spectroscopy in accordance with an embodiment of the present invention.

Figures 15A and 15B illustrate the preparation of a cleavable tag of the present invention.